UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/308,223	08/12/99	KALLMEYER G	P8341-9011

HM22/1016
NIKAIDO MARMELSTEIN MURRAY AND ORAM
METROPOLITAN SQUARE
655 FIFTEENTH STREET NW
SUITE 330 G STREET LOBBY
WASHINGTON DC 20005-5701

EXAMINER	
NICKOL,G	
ART UNIT	**PAPER NUMBER**
1642	9

DATE MAILED: 10/16/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/308,223	KALLMEYER ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☒ Responsive to communication(s) filed on *13 July 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-21,23-32 and 34-36* is/are rejected.

7)☒ Claim(s) *22 and 33* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☒ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☒ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

Response to Amendment

The Amendment filed July 13, 2000 (Paper No. 8) in response to the Office Action of January 19, 2000 is acknowledged and has been entered. Claims 13-36 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 26 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 26 is rejected as indefinite as being structured as an improper Markush claim in that the groups within the Markush claim do not share both a common utility and a common structural feature. See MPEP 803.02.

Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d 461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject

matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claim 36 is rejected under 35 U.S.C. 102(e) as being anticipated by Fukuda et al. (US Patent No. 5,908,826, 1992).

The claim is drawn to a method of preparing a lyophilizate, comprising mixing a buffered solution containing a monoclonal antibody or a polyclonal antibody, a sugar or an amino sugar, at least one amino acid and a surfactant, to prepare a mixed solution, wherein the mixed solution has a pH value of 5-8; and lyophilizing the mixed solution.

Fukuda et al. teach a method of preparing a lyophilizate, comprising mixing a buffered solution containing a monoclonal antibody (column 4, lines 35-41), a sugar or an amino sugar (column 4, lines 45-49) at least one amino acid (column 4, line 52) and a surfactant (column 5, line 30), wherein the mixed solution has a pH value of 5-8 (column 5, line 9).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13- 21, 23-32, and 34-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Phillips et al (WO 89/11297) in view of Friedman et al. (US Patent No. 5750142) and Arizono et al. (Arzneimittelforschung, Vol. 44, No. 7, 1994).

The claims are drawn to a lyophilizate comprising a monoclonal or polyclonal antibody, a sugar or an amino sugar, at least one amino acid, and a surfactant, wherein the lyophilizate is essentially free of polyethylene glycols (PEGs) (Claim 13); wherein the lyophilizate is essentially free of additional proteins(Claim 14); wherein the lyophilizate contains a single

amino acid or two different amino acids (Claim 15); wherein the lyophilizate further comprises a buffering agent or an isotonizing agent which is present in an amount such that a reconstituted solution of the lyophilizate has a pH value of 5-8 (claim 16); wherein the lyophilizate is storage-stable for a time period of at least three months at a temperature of about 4-12C (Claim 17) or a temperature of about 18-23C(Claim 18);

The claims are further drawn to the lyophilizate wherein the sugar comprises at least one member selected from the group consisting of a monosaccharide, a disaccharide, and a trisaccharide (Claim 19); wherein the sugar comprises at least one member of those listed in (Claims 20 and 21); wherein the amino acid comprises at least one member selected from those listed in (Claim 23); wherein the surfactant comprises a polysorbate or a polyoxyethylene-polyoxypropylene polymer (Claim 24); wherein the monoclonal or the polyclonal antibody has a molecular weight of 50-200 kDa per monomer unit (claim 25); wherein the monoclonal or polyclonal antibody is directed against an antigen selected from the groups in (Claim 26); a liquid pharmaceutical composition comprising the lyophilizate of Claim 13 dissolved in a physiologically acceptable solution (Claim 28); wherein the liquid pharmaceutical composition has a pH value of 5-8 (Claim 29); contains 1-10mg/ml of antibody (Claim 30); and further contains up to 200 mg/ml of sugar or amino sugar (Claim 31); up to 100 mg/ml of amino acid (Claim 32).

The claims are further drawn to a lyophilizate consisting essentially of a monoclonal or polyclonal antibody, a sugar or an amino sugar, at least one amino acid, a surfactant, and an inorganic acid as a buffering agent (Claim 27); which further comprises a liquid pharmaceutical

composition dissolved in a physiologically acceptable solution (Claim 34); which has a pH value of 5-8 (Claim 35).

1. Phillips et al. teaches a lyophilizate (and a method of preparing such) comprising a monoclonal antibody, a sugar, and an inorganic buffering agent (page 7, line 20) which is essentially free of PEGs and or additional proteins. Phillips et al. teach that buffer has a pH of between "about" 3-6. Phillips et al. teach that the sugar comprises a disaccharide, which is maltose. Phillips et al. teach the lyophilizate is storage stable for a time period of at least three weeks at a temperature of about 4-12C or 18-23C (pages 10-12, and 19). Phillips et al. teach that the monoclonal antibody has a molecular weight of 5-200 kDa per monomer unit (IgG is approximately 150 kDa as known in the art). Phillips et al. further teach a liquid pharmaceutical composition comprising the lyophilizate dissolved in a physiologically acceptable solution containing 1-10mg/ml of antibody (page 7, line 24), and up to 200 mg/ml of sugar or up to 20%. Phillips et al teach that the amount of maltose is between about 2-10% by weight.
2. Phillips et al. do not include at least one amino acid and a surfactant.
3. Friedman et al. (U.S. Patent No. 5,750,142) teach an improved lyophilizate comprising an antibody (column 19, line 30), at least one amino acid (column 3, lines 55-65) or two or more different amino acids (column 4, line 1) at a concentration ranging up to 100mg/ml of amino acid or 10% wherein Friedman et al. teach a range from about 0.25 to 25% (column 4, line 11) and a surfactant (column 5, lines 11-44).

4. Arizono et al. teach a lyophilized monoclonal antibody directed against an antigen selected from the group consisting of cytomegalovirus (abstract only).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to optimize the lyophilizate of Phillips et al. to include amino acids and a surfactant as taught by Friedman et al. in order to obtain an improved lyophilizate having a long shelf-life. One would have been motivated to include such compounds in the lyophilizate of Phillips et al. because Friedman et al teach that the inclusion of amino acids provides superior performance with respect to the droplet size of the reconstituted product (column 2, line 27) and the addition of surfactants can be used to enhance the formation of the emulsion (column 5, line 12). Further, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the antibody used by Phillips et al. with an antibody directed against an antigen associated with a particular disease since Phillips et al teach that the antibody of choice can be used for in vivo diagnostic imaging of disease sites (page 7, line 10). Further, one would have been motivated to use an antibody directed against a particular disease in view of the successful teachings of Arizono et al.(see abstract).

Claim Objections

Claims 22 and 33 are objected to because they depend from a rejected base claim. Amendments or cancellations are necessary to obviate the objections.

All previous rejections recited in the Office Action of January 19, 2000 (Paper No. 6) are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
October 3, 2000

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600